

**IN THE UNITED STATES DISTRICT COURT  
NORTHERN DISTRICT OF IOWA  
WESTERN DIVISION**

<b>MARLIN HERBST,</b>	)	
	)	
	)	
<b>Plaintiff,</b>	)	<b>Case No. 5:17-cv-04008-MWB</b>
	)	
<b>v.</b>	)	
	)	
<b>BUSH BOAKE ALLEN INC., et al.</b>	)	
	)	
<b>Defendants.</b>	)	

**PLAINTIFF’S OPPOSITION TO DEFENDANT GIVAUDAN FLAVORS  
CORPORATION’S FIRST *DAUBERT* MOTION TO EXCLUDE GENERAL  
CAUSATION TESTIMONY BY PLAINTIFF’S EXPERT**

COME NOW Plaintiff and files this opposition to Givaudan’s<sup>1</sup> First *Daubert* Motion to Exclude General Causation Testimony by Plaintiff’s Expert. Respectfully, the motion must be denied.

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<sup>1</sup> Defendant Emoral, Inc., f/k/a Polarome International, Inc. (“Emoral”) joined in Givaudan’s motion. Plaintiff respectfully asks this Court deny the motion as it relates to Emoral as well.

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## I. INTRODUCTION

Dr. Harrison's opinion that diacetyl causes the lung disease bronchiolitis obliterans is admissible because he relies on a wealth of peer-reviewed literature as well as his own independent analysis based on scientifically-accepted methodology. For over fifteen years, scientists and physicians have been publishing peer-reviewed articles containing their conclusion that diacetyl causes bronchiolitis obliterans. In 2016, the National Institute for Occupational Safety and Health ("NIOSH") published a 400-page report detailing the science and medicine supporting its conclusion that diacetyl exposure in the workplace causes this same disease. Dr. Harrison not only relies on this report and the original investigations, studies, and peer-reviewed articles it cites, but he also independently confirmed general causation by applying the Bradford Hill criteria. Both the scientific community and federal courts recognize that the Bradford Hill criteria are a widely-accepted and scientifically sound method to determine causation. Under *Daubert*, Dr. Harrison's opinions are sufficiently supported by science. It would be an abuse of discretion and reversible error to exclude them.

Federal courts, including this Court, have already addressed this specific issue and agree with NIOSH's conclusion that the science supports general causation. In 2013, this Court denied a near-identical *Daubert* motion in a case involving the same chemical and the same disease as this case. In doing so, this Court steered clear from violating the Eighth Circuit's mandate that *Daubert* calls for the liberal admission of expert testimony. And just last month the Seventh Circuit reversed a district court's entry of summary judgment and held that the plaintiffs are entitled to a trial on whether or not Givaudan's butter flavors caused their lung disease. Yet Givaudan nonetheless asks this Court to be the first in the nation to hold that diacetyl cannot cause lung disease in worker's who are exposed to it. This Court should deny Givaudan's

motion. Dr. Harrison's methodology is sound, and his conclusions are shared by the overwhelming majority of both the scientific and medical communities.

## II. LEGAL AUTHORITY

### A. **The Eighth Circuit admonishes district courts to not weigh the competing opinions of experts and instead requires them to liberally admit all scientific testimony.**

The Eighth Circuit has repeatedly emphasized that the district courts should exercise their gate-keeping function pursuant to Rule 702 and *Daubert* to exclude only evidence that is fundamentally unsupported by any scientific methodology. Absent this high threshold, courts must liberally admit expert opinion and permit any flaws to be addressed via cross examination:

While we adhere to this discretionary standard for review of the district court's Rule 702 gatekeeping decision, cases are legion that, correctly, under *Daubert*, call for the liberal admission of expert testimony. *See, e.g., United States v. Finch*, 630 F.3d 1057, 1062 (8th Cir.2011) (holding that we resolve doubts about the usefulness of expert testimony in favor of admissibility); *Robinson v. GEICO Gen. Ins. Co.*, 447 F.3d 1096, 1100 (8th Cir.2006) (holding that expert testimony should be admitted if it "advances the trier of fact's understanding to any degree" (quotation omitted)); *Lauzon v. Senco Prods., Inc.*, 270 F.3d 681, 686 (8th Cir.2001) (Rule 702 "clearly is one of admissibility rather than exclusion" (internal quotation omitted)); *Wood v. Minn. Mining & Mfg. Co.*, 112 F.3d 306, 309 (8th Cir.1997) (holding that exclusion of expert's opinion is proper "only if it is so fundamentally unsupported that it can offer no assistance to the jury" (internal quotation omitted)). Further, district courts are admonished not to weigh or assess the correctness of competing expert opinions. *Wyeth*, 686 F.3d at 625. As long as the expert's scientific testimony rests upon "good grounds, based on what is known" it should be tested by the adversary process with competing expert testimony and cross-examination, rather than excluded by the court at the outset. *Daubert*, 509 U.S. at 590, 596, 113 S.Ct. 2786.

*Johnson v. Mead Johnson & Co., LLC*, 754 F.3d 557, 562 (8th Cir. 2014). Attacks directed at the factual basis for expert opinion generally give rise to issues of credibility, not admissibility. *Tussey v. ABB, Inc.*, 746 F.3d 327, 337 (8<sup>th</sup> Cir. 2014) (additional citations omitted). "Only if the expert's opinion is so fundamentally unsupported that it can offer no assistance to the jury must such testimony be excluded." *Osment Models, Inc. v. Mike's Train House, Inc.*, 2010 WL

4721223, at \*2 *quoting Wash Solutions, Inc. v. PDQ Mfg., Inc.*, 395 F.3d 888, 895 (8<sup>th</sup> Cir. 2005) (additional citations omitted). Credibility issues are properly addressed through cross-examination by the opposing party. *Id.*

In 2001, the Eighth Circuit held it is reversible error not to permit an expert to testify to an opinion that is supported by peer-review articles and generally accepted by the relevant scientific community. *Lauzon v. Senco Products, Inc.*, 270 F.3d 681 (8th Cir.2001). The *Lauzon* court explained that an expert is not required to rule out all other possible causes of an injury before he can offer opinions on causation. Instead, because the expert's based his opinions on reliable methodology, the court must allow the jury to determine their credibility:

Senco may attack Kelsey's explanations of causation on cross examination, thereby requiring Kelsey to offer valid explanations as to why his conclusion remains reliable. *See McCulloch v. H.B. Fuller Co.*, 61 F.3d at 1038, 1044 (2d Cir.1995). To hold otherwise denigrates Justice Blackmun's observation in *Daubert*: "In this regard respondent seems to us to be overly pessimistic about the capabilities of the jury and of the adversary system generally. Vigorous cross-examination, presentation of contrary evidence, and careful instruction on the burden of proof are the traditional and appropriate means of attacking shaky but admissible evidence."

*Lauzon*, 270 F.3d, at 694 (quoting *Daubert v. Merrell Dow Pharm., Inc.*, 509 U.S. 579, 596 (1993)).

*Lauzon* is not an outlier – the Eighth Circuit has repeatedly confirmed that attacks such as Givaudan's do not affect the admissibility of an expert's opinions. In fact, even when no published article on causation exists, the Eighth Circuit still permits an expert to offer causation opinions: **"There is no requirement that a medical expert must always cite published studies on general causation** in order to reliably conclude that a particular object caused a particular illness . . . [I]ikewise, **there is no requirement that published epidemiological studies supporting an expert's opinion exist in order for the opinion to be admissible.**" *Bonner v.*



*ISP Techs., Inc.*, 259 F.3d 924, 929 (8th Cir. 2001) (emphasis added). Here, of course, over a decade of such published studies exist. Givaudan has no legal grounds to exclude Dr. Harrison's opinions.

**B. Just last month the Seventh Circuit held that plaintiff's experts, including Dr. Harrison, can opine on the universally accepted science that diacetyl causes bronchiolitis obliterans.**

On September 13, 2018, the Seventh Circuit overturned summary judgment in Givaudan's favor in a case involving diacetyl and bronchiolitis obliterans. (Exh. 1, *Aregood v. Givaudan Flavors Corp.*, No. 17-3390, 2018 WL 4355591 (7th Cir. Sept. 13, 2018)) The Seventh Circuit held that the plaintiffs, all employees in a microwave popcorn plant, had a right to trial on their failure to warn claims: "Whether an exception to that duty to warn—the sophisticated intermediary doctrine—applies to the employer ConAgra and exonerates Givaudan is a fact question, so **we remand for trial on that claim.**" *Id.* at \*1 (emphasis added). The Seventh Circuit did not blink at the admissibility of Drs. Parmet, Pue, or Harrison's opinions:

In support of their claims, the employees have offered opinions of various expert witnesses. An occupational physician [Dr. Parmet] opined that the levels of diacetyl in the air at the Rensselaer plant when plaintiffs worked there likely caused bronchiolitis obliterans. Another doctor [Dr. Pue] examined the plaintiffs and diagnosed them with flavoring-induced bronchiolitis obliterans caused by exposure to diacetyl at the Rensselaer plant. An epidemiologist and occupational physician [Dr. Harrison], who had reviewed the documentary and testimonial record, opined Givaudan should have known that diacetyl caused lung disease, as well as that Givaudan withheld from ConAgra the health risks of its butter flavoring.

*Id.*

There, Givaudan presented the Seventh Circuit with a near-identical *Daubert* motion seeking to exclude the plaintiffs' experts' opinions on general causation: "Moreover, the expert opinions on general and specific causation that Appellants point to are unreliable and inadmissible for the reasons stated in Givaudan's second and third *Daubert* motions." (Exh. 2,

Givaudan’s Appellee Brief, p. 28, fn9) Givaudan repeated this argument at the end of its brief: “The district court’s entry of summary judgment as to all of Appellants’ claims should also be affirmed because, as described in Givaudan’s motions to exclude (Dkt. Nos. 494, 496, 498, 499, 541, 542), Appellants’ medical experts’ opinions are unreliable and inadmissible and, therefore, Appellants lack the requisite causation evidence.” *Id.*, p. 46 fn14.

The Seventh Circuit was not impressed with Givaudan’s arguments or its *Daubert* motions. In fact, it did not even question whether diacetyl causes bronchiolitis obliterans. While acknowledging that specific causation remained an unproven allegation in the case, it recited without hesitation the reality that diacetyl causes this disease and its accompanying symptoms: “Exposure to diacetyl, the employees allege, resulted in their developing respiratory illnesses. When inhaled, diacetyl can cause bronchiolitis obliterans—commonly referred to as ‘popcorn lung’—the inflammation and obstruction of the smallest airways of the lungs. Symptoms of this disease include a dry cough, shortness of breath, wheezing, fatigue, and can lead to worse personal injuries.” (Exh. 1, *Aregood*, 2018 WL 4355591, at \*1) The Seventh Circuit even declares in its opening sentence that diacetyl’s ability to cause lung disease is not a question: “More than twenty current and former employees at the ConAgra microwave popcorn plant in Rensselaer, Indiana sued various manufacturers and suppliers of butter flavorings that contained the chemical diacetyl, **which if inhaled can cause a respiratory disease called ‘popcorn lung.’**” *Id.* (emphasis added). The Seventh Circuit rejected Givaudan’s arguments that these experts cannot opine on general causation, and so should this Court.

**C. This Court has already recognized that general causation is a question of fact for the jury.**

Consistent with both the mandate from the Eighth Circuit, and the most recent opinion from the Seventh Circuit, this Court has previously rejected a general causation challenge from

Givaudan. (Exh. 3, February 5, 2013 Order Regarding Defendants’ Motions To Exclude Opinions of Expert Witnesses in *Daughetee v. Chr. Hansen, Inc., et al.*, Case No. C09-4100-MWB (Doc. 317)) In *Daughetee*, Givaudan filed *Daubert* motions seeking to exclude “plaintiffs’ experts’ opinions concerning general and specific causation on the grounds that their opinions are not scientific, reliable, and/or relevant.” *Id.* at \*1. This Court quickly denied the motions, easily concluding that Givaudan failed to present any legitimate basis to exclude the opinions:

I find it unnecessary to hold oral arguments on the motions or, indeed, to await plaintiffs’ responses to the motions. Defendants’ “Daubert” challenges will be considered at trial because I conclude this case is one in which “vigorous cross-examination, presentation of contrary evidence, and careful instruction on the burden of proof are not only traditional, but appropriate means of attacking what [the opponent of the evidence] contends is shaky evidence.”

*Id.* at \*1-2, (quoting *Kuiper v. Givaudan, Inc.*, 602 F. Supp.2d 1036, 1057 (N.D. Iowa 2009)).

This Court should not depart from its sound rulings in *Daughetee* and *Kuiper*. Dr. Harrison’s general causation opinions are admissible.

### III. ARGUMENT

#### A. For over a decade, courts have recognized the evidentiary value of general causation opinions in these type of cases.

Courts of various jurisdictions around the country have repeatedly admitted expert testimony on “general causation.” This is because the scientific, medical, and public health communities all agree that exposure to butter flavorings containing diacetyl is capable of causing lung disease, including bronchiolitis obliterans. In fact, more than ten years ago, Givaudan itself conceded causation. In 2007, Givaudan began warning its customers that its butter flavorings containing diacetyl caused permanent lung disease:

- “Repeated or prolonged exposure to the substance can produce lung damage.”
- “Very hazardous in case of inhalation.”

- “HARMFUL IF INHALED. Harmful: possible risk of irreversible effects through inhalation.”

(Exh. 4, at pp. 2 and 4.)<sup>2</sup> Givaudan was not alone in conceding causation. Emoral began warning its customers as far back as 2004 that: “**PROLONGED EXPOSURE TO HIGH CONCENTRATIONS MAY CAUSE LUNG DISEASE, BRONCHIOLITIS OBLITERANS.**” Exh. 52, November 30, 2004, Polarome material safety data sheet (emphasis in original).

As even Emoral concedes, there is no genuine dispute that exposure to diacetyl causes bronchiolitis obliterans. Givaudan has litigated these cases for almost a decade, and in many of these cases the plaintiffs have relied on testimony from Drs. Parmet<sup>3</sup> and/or Harrison. Yet Givaudan has never challenged these experts or their methods for general causation until just recently. These challenges have never succeeded – no court has ever excluded these experts from offering general causation opinions. In fact, by Plaintiff’s count there are at least thirty-six (36) instances in which a plaintiff in a diacetyl-related case has relied on Dr. Parmet to provide general causation opinions. And all 36 times, the court permitted him to testify. In most of these cases Givaudan was a named defendant. The overwhelming majority involve flavor industry workers just like Mr. Herbst. Those cases:

1. *Arnold v. IFF, Inc., & Givaudan, et al.* in the Court of Common Pleas, Marion County, Ohio
2. *Arthur v. International Flavors & Fragrances, Inc., et al.*, In the Court of Common Pleas, Hamilton County, Ohio, Case No. A0307157
3. *John Weimer, Jr., v. International Flavors & Fragrances, Inc., et al.*, N.D. Iowa, Western Division, Case No. C05-4138 DEO

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<sup>2</sup> Givaudan was not alone in conceding causation. Emoral began warning as far back as 2004 that: “**PROLONGED EXPOSURE TO HIGH CONCENTRATIONS MAY CAUSE LUNG DISEASE, BRONCHIOLITIS OBLITERANS.**” (Exh. \_\_\_, November 30, 2004 Polarome material safety data sheet (emphasis in original))

<sup>3</sup> As Givaudan points out, while Plaintiff has not retained Dr. Parmet, his peer-reviewed articles are among the extensive literature Dr. Harrison relies on to support his general causation opinion.

4. *Arturo Lopez v. Flavors of North America, Inc., et al.*, Circuit Court of Cook County, IL, Case No. 04 L 7262
5. *Christopher Blood v. International Flavors & Fragrances, Inc.*, In the Court of Common Pleas, Hamilton County, Ohio, Case No. A0700449
6. *George Aldrich II v. International Flavors & Fragrances, Inc., et al.*, In the Court of Common Pleas, Hamilton County, Ohio, Case No. A0700451
7. *Brad Arnold v. International Flavors & Fragrances, Inc., et al.*, In the Court of Common Pleas, Hamilton County, Ohio, Case No. A0704947
8. *Leslie Adamson v. International Flavors & Fragrances, Inc.*, In the Court of Common Pleas, Hamilton County, Ohio, Case No. A0706062
9. *Robert Ferguson v. International Flavors & Fragrances, Inc., et al.*, In the Court of Common Pleas, Hamilton County, Ohio, Case No. A0803169
10. *Brian Brown v. International Flavors & Fragrances, Inc., et al.*, In the Court of Common Pleas, Hamilton County, Ohio, Case No. A0803190
11. *Chris Harper v. Givaudan Flavors Corp.*, In the Court of Common Pleas, Hamilton County, Ohio, Case No. A1000229
12. *Elizabeth Fults v. International Flavors & Fragrances, Inc., et al.*, 23<sup>rd</sup> Judicial Circuit Court, Missouri, Case No. 06PR-CC00028-01
13. *Jason Byrd v. International Flavors & Fragrances, Inc., et al.*, Circuit Court, Jasper County, Missouri, Case No 06AP-CC00084-04
14. *Vonnie Davis v. International Flavors & Fragrances, Inc., et al.*, Circuit Court, Jasper County, Missouri, Case No 06AP-CC00084-09
15. *Jeannie Ellis v. International Flavors & Fragrances, Inc., et al.*, Circuit Court, Jasper County, Missouri, Case No 06AP-CC00084-10
16. *James Leedy v. International Flavors & Fragrances, Inc., et al.*, Circuit Court, Jasper County, Missouri, Case No 06AP-CC00084-17
17. *Rita Mitchell v. International Flavors & Fragrances, Inc., et al.*, Circuit Court, Jasper County, Missouri, Case No 06AP-CC00084-20
18. *DeEnna Stebler v. International Flavors & Fragrances, Inc., et al.*, Circuit Court, Jasper County, Missouri, Case No 06AP-CC00084-29
19. *Kevin Blades v. International Flavors & Fragrances, Inc., et al.*, Circuit Court, Jasper County, Missouri, Case No 06AP-CC00084-30
20. *Estate of Dennis Yatsko's v. Ventura Foods, LLC, et al.*, District Court, Cascade County, Montana, Case No. CDV 05 701
21. *Eric Peoples v. International Flavors & Fragrances, et al*
22. *Linda Redman v. IFF and BBA*, Jasper County, MO,
23. *Dustin Smith, et al. v. IFF and BBA*, Jasper County, MO
24. *Louis Pennell v. IFF and BBA*, Jasper County, MO

25. *Richard Brand v. IFF and BBA*, Jasper County, MO
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27. *Stephen McNeely v. IFF and BBA*, Jasper County, MO
28. *Jerry Blaylock v. Sigma Aldrich, Inc., et al.*, Circuit Court of City of St. Louis, MO
29. *Ronald Kuiper v. Givaudan Flavors*
30. *Kathryn Rayburn v. Givaudan Flavors*
31. *Gerardo Solis v. BASF Corporation*
32. *Brian Hallock v. Polarome International, Inc.*
33. *Wayne Watson v. Dillon Companies, Inc., et al.*, United States District Court for District of Colorado<sup>4</sup>
34. *Stults v. International Flavors & Fragrances, Inc.*, United States District Court, Northern District of Iowa, Western Division
35. *Doane, et al v. Givaudan, et al, Court of Common Please, Hamilton County*, Case No. A-0700452
36. *Chavez v. Givaudan, et al*, Superior Court of the State of California, Case No. BC482678

Likewise, plaintiffs across the country have relied on Dr. Harrison to offer general causation opinions. And again, only very recently has Givaudan filed *Daubert* challenges against his opinions. None of them have been successful. Any legitimate scientific disagreement with the reality that diacetyl causes lung disease, even if it existed (and it does not), is grounds to cross-examine Dr. Harrison, not to exclude his testimony.

**B. Dr. Harrison is a highly qualified occupational health physician with years of experience and service dedicated to identifying, preventing, and treating occupational diseases including Flavor Induced Bronchiolitis Obliterans.**

Dr. Harrison is highly qualified to offer opinions on the well-accepted conclusion, based on sound principles and methods, that diacetyl causes bronchiolitis obliterans. Givaudan

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<sup>4</sup> In *Watson*, a consumer case (the Plaintiff was exposed to diacetyl vapors by cooking popcorn at home), the defendants moved to exclude both the general and specific causation opinions of several Plaintiff experts, including Dr. Parmet, and for summary judgment. The District Court for the District Court of Colorado engaged in a specific *Daubert* analysis, permitted days of hearings specific to *Daubert* issues, and then denied the motions and ordered the parties to trial. The jury returned a verdict in excess of \$7,000,000 for Plaintiff. The *Watson* Court's Order denying summary judgment and motions to exclude is attached here as Exh. 5.

concedes that he is qualified, yet his extensive training, experience, and history are still relevant to this Court's determination that he can offer general causation opinions. Robert Harrison, M.D., M.P.H., is a medical doctor and Clinical Professor of Medicine at the University of California at San Francisco. (Exh. 6, CV of Robert Harrison, M.D., M.P.H.) He is a visiting professor in the School of Public Health at the University of California at Berkeley. He is board certified in occupational medicine and internal medicine and holds a Master's in Public Health. He has more than 30 years of experience in the determination of whether chemical exposure is likely to cause disease among working populations, the design and implementation of workplace programs to prevent occupational diseases caused by workplace chemicals, and the detection of disease outbreaks in the workplace that has led to both public health and regulatory changes.

Dr. Harrison's specific experience with bronchiolitis obliterans makes him especially qualified to offer general causation opinions in this case. He served as Chief of the Occupational Health Surveillance and Evaluation Program of the California Department of Public Health. While in that position he published the first two cases of bronchiolitis obliterans caused by exposure to diacetyl in the food flavorings industry in California. (Exh. 7, Harrison, R: et al. (2006) *Food flavoring workers with bronchiolitis obliterans following exposure to diacetyl, California*, May 15, 2006). Dr. Harrison's qualifications are impeccable and unquestioned; there is no doubt he is qualified to offer general causation opinions in this case.

**C. Dr. Harrison's opinions are based on reliable methods because they are supported by over a decade of peer-reviewed literature as well as his own independent and scientifically sound analysis.**

Dr. Harrison provides a sufficiently reliable basis to support his opinions. He has issued thorough and detailed reports, both in this case and others. (Exh.8, Report of Dr. Harrison for Marlin Herbst. *See also* Exh. 9, Dr. Harrison's Report in the *Aregood* case) In reaching his

opinions, Dr. Harrison considered published epidemiologic reports, relevant human case reports, animal data, experimental studies, laboratory data, mechanistic data, and other types of data as well, including unpublished studies. (Exh. 8, *see also* Exh. 9 and Exh. 10, Harrison Dep., Ruby, 11:20-12:12). These materials are scientifically valid and date back to 2002. Dr. Harrison provided an extensive reference list, identifying this wealth of literature he basis his opinions on. (Exh. 51, Harrison Reference list). As Dr. Harrison explained to Givaudan's counsel in deposition, researching and relying upon peer-reviewed literature is not just something he does as a witness; it is the backbone of occupational medicine. (Exh. 10, Harrison Dep, Ruby, 240:17-25; 241:13-18).

In addition to relying upon the scientific and medical literature, Dr. Harrison also performed his own independent analysis by applying the Bradford Hill criteria. (Exh. 9) Federal courts have routinely recognized that the scientific community has universally accepted the Bradford Hill criteria as an accurate method to determine causation. Dr. Harrison explains in his report that diacetyl's ability to cause lung disease meets each of the criteria (which Dr. Hill called "viewpoints"): consistency, strength of the observed association, specificity of the observed association, temporal relationship of the observed association, biologic gradient (exposure-response relationship), biologic plausibility, coherence, experimental evidence (from human populations) and analogy. *Id.* Dr. Harrison exhaustively set forth facts and studies that support each criteria or "viewpoint" of the Bradford Hill criteria demonstrating that diacetyl does cause lung disease. Dr. Harrison's use of peer-reviewed literature and the Bradford Hill criteria comports with generally accepted scientific methodology and is sufficiently reliable to satisfy *Daubert*. Defendants' motion to exclude Dr. Harrison must be denied.



**1. The case body of scientific, medical, and government literature supporting Dr. Harrison's opinions is overwhelming.**

By 2007, the scientific literature detailing diacetyl's propensity to cause lung disease had become so overwhelming that Givaudan had no choice but to acknowledge it on the MSDS it supplied with diacetyl-containing products. (Exh. 4). In the decade since, the case against diacetyl has only grown stronger. In 2016, the National Institute of Occupational Safety and Health (NIOSH) published a 400-page report on its nearly two-decade long investigation of diacetyl. In its report, NIOSH details the scientific and medical research on the matter and concludes that diacetyl causes the same lung disease that Mr. Herbst suffers from. Dr. Harrison relies on this report, as well as the wealth of peer-reviewed articles and studies on the matter. Givaudan's request to exclude his general causation opinions is absurd.

**a) NIOSH's Findings Conclusively Establish General Causation**

NIOSH has studied this issue for approximately 17 years, since Dr. Parmet – the very occupational physician whose articles Givaudan asks this Court to discredit – first reported his observation of an epidemic of bronchiolitis obliterans at a Missouri microwave popcorn plant. Since 2000, NIOSH has conducted Health Hazard Evaluations at numerous food manufacturing facilities including microwave popcorn and food flavoring manufacturing plants; conducted animal studies; conducted studies of diacetyl emission from a variety of flavor products; sought expertise from outside NIOSH and reviewed the scientific peer-reviewed literature on diacetyl and lung disease. NIOSH has authored peer-reviewed articles of original research into this subject. This research culminated in November 2016 when NIOSH published its 400-page *Criteria for a Recommended Standard: Occupational Exposure to Diacetyl and 2,3-pentanedione*, by McKernan, LT, et. al, Cincinnati, OH: U.S. Department of Health and Human

Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 2016-111. (Exh. 11, “NIOSH Criteria Report”).

In this publication, NIOSH states directly:

Investigations of severe lung disease consistent with obliterative bronchiolitis among diacetyl-exposed employees have provided substantial evidence of a causal relationship between diacetyl exposure and development of this disease. Exposure preceded disease development, and lung disease risk decreased with control of exposures. Analyses of data from workplace medical and environmental surveys revealed a strong, consistent association of the disease with diacetyl manufacture, use of diacetyl in flavoring production, and use of diacetyl-containing butter flavorings in microwave popcorn production. The investigations have also shown evidence of a dose-response effect, and animal and other laboratory studies have provided evidence of biologic plausibility. Medical evaluations of affected employees did not identify alternative explanations for their illness besides their workplace exposure to diacetyl and other flavoring compounds. Accordingly, the criteria for interpreting epidemiologic associations as causal have all been met by the body of investigation presented in this criteria document for a recommended standard.

*Id.* at p. 74.

The NIOSH Criteria Report is a complete scientific report of the federal government’s investigation into diacetyl with a detailed explanation of its research and conclusions. It is ten chapters in length. It provides a detailed history of the investigation of diacetyl related lung disease in the food flavoring industry and an excellent summary of the history of diacetyl research:

Diacetyl is used extensively in the food flavoring and production industries, and occupational exposure to this substance has been associated with severe respiratory impairment and the disease obliterative bronchiolitis. 2,3-Pentanedione, which has been used as a substitute for diacetyl, is also of concern because of structural similarities with diacetyl and because animal studies show similar toxicity for the respiratory tract [Hubbs et al. 2012; Morgan et al. 2012; Morgan et al. 2016].

The first observation of obliterative bronchiolitis in a food production employee may have occurred in 1985 in a facility where diacetyl was listed among ingredients used in making flavorings for the baking industry [NIOSH 1985]. The link between exposure to diacetyl and lower pulmonary function was confirmed

in the early 2000s, and research further showed that diacetyl exposure leads to a decrease in pulmonary function [Kreiss et al. 2002]. Occupational exposures to diacetyl have been assessed in a variety of food production and flavoring facilities [Kanwal et al. 2006; Martyny et al. 2008; NIOSH 2003a, b, 2004a, b, 2006, 2007, 2008a, b, 2009, 2011].

Mean diacetyl air concentrations measured at the first microwave popcorn facility where obliterative bronchiolitis was reported were highest in the mixing room (57.2 parts per million [ppm]), followed by the packaging area (2.8 ppm) [Kanwal et al. 2011]. Mean personal diacetyl air concentrations at five other microwave popcorn plants were lower: 0.023 to 1.16 ppm in the mixing room and 0.35 to 1.33 ppm in the packaging rooms/areas [Kanwal et al. 2006]. Mean full-shift diacetyl air concentrations measured at flavor manufacturing facilities ranged from 0.07 ppm to 2.73 ppm [Kanwal et al. 2006; Martyny et al. 2008; NIOSH 2003a, b, 2004a, b, 2006, 2007, 2008a, b, 2009, 2011].

In addition to cases consistent with obliterative bronchiolitis in flavoring manufacturing, diacetyl manufacturing, and microwave popcorn production, case reports have surfaced in other industries in which flavorings are introduced. In cookie manufacturing with artificial butter flavoring in Brazil, four cases of bronchiolitis were described in young men, aged 24 to 27 years, who had worked between 1 and 3 years handling flavorings in preparation of cookie dough [Cavalcanti et al. 2012]. In a coffee production plant, two cases have biopsy confirmation of obliterative bronchiolitis among employees with artificial flavorings exposure in the production of roasted coffee beans and ground coffee [CDC 2013]. In 2012, NIOSH conducted a health hazard evaluation (HHE) involving 75 current employees (88% participation) [Bailey et al. 2015]. Excluding the five sentinel former employees (all never-smokers under age 42), standardized morbidity ratios were elevated 1.6-fold for shortness of breath and 2.7-fold for obstructive spirometric abnormalities.

**Investigations of severe lung disease consistent with obliterative bronchiolitis among diacetyl-exposed employees presented in Chapter 3 have provided substantial evidence of a causal relationship between diacetyl exposure and development of this disease. These findings in conjunction with laboratory experiments providing biological plausibility, meet the standard criteria used to determine causation: that an exposure is the likely cause of specific health effects [Gordis 1996; Hill 1965].**

NIOSH has reviewed the literature on diacetyl toxicology and exposures in the workplace and subsequently conducted a quantitative risk assessment. The quantitative risk assessment used to derive the REL was based solely on human (employee) data, but the results were informed and corroborated by animal risk assessments. On the basis of a quantitative risk assessment of data collected in a series of NIOSH health hazard investigations (full description in Chapter 5), NIOSH has concluded that employee exposure to diacetyl is associated with a

reduction in lung function. Specifically, a statistically significant exposure-associated reduction in the forced expiratory volume in one second/forced vital capacity (FEV1/FVC) ratio and percent predicted FEV1 (ppFEV1) and an exposure-associated estimated incidence of symptomatic obstructive lung disease were observed. NIOSH quantified these exposure- response relationships and determined the exposure levels that correspond to a variety of risks (Chapter 5, Table 5.35). Lifetime risks in the range of 1:1,000 corresponded to working lifetime diacetyl exposure of approximately 5 parts per billion (ppb). Once the risks were characterized, NIOSH examined the analytical methods (OSHA Methods 1012 and 1016) and available engineering controls and determined that they supported establishing a REL at that level.

**NIOSH concludes that the toxicological responses to diacetyl observed in animal studies support the conclusions of the epidemiologically-based risk assessment for diacetyl.** Further, the animal-based risk assessment presented in Chapter 6 corroborates the epidemiologic assessment by demonstrating a causal link between diacetyl exposure and respiratory health effects and by showing a clear dose- response relationship in exposed animals as was observed in employees exposed to diacetyl in the epidemiologic assessment.

*Id.* at pp. v – vii).

While the NIOSH Criteria Report was authored by the scientists listed above, many other scientists have assisted NIOSH. *Id.* at pp. xxvii-xxviii. Six divisions within NIOSH assisted in the research and authorship of the publication including:

- Division of Applied Research and Technology,
- Respiratory Health Division,
- Division of Surveillance, Hazard Evaluations, and Field Studies,
- Education and Information,
- Health Effects Laboratory Division and
- National Personal Protective Technology Laboratory.

*Id.*

Before publishing this Criteria Report, NIOSH submitted a draft document for public review in 2011. That draft document was the subject of meetings of both the public and the scientific community. NIOSH invited comments to the draft and even extended the period for comments to ensure full and fair feedback from the public. NIOSH responded in writing to those

comments and has made those comments and responses available to the public.<sup>5</sup> Like scientific articles published in journals, the NIOSH Criteria Report was the subject of extensive and independent peer-review. (Exh. 11, at p. xxvii).<sup>6</sup> Only after this extensive comment and editing period concluded was the final Criteria Document published.

The Criteria Document is the result of lengthy and detailed work for the public good, by a governmental agency tasked with protecting the working public. It is the culmination of many years of study and investigation at various facilities around the country, including the very facility where Plaintiff Marlin Herbst worked. Givaudan does not attack the methodology of the Criteria Report. Instead of acknowledging NIOSH's findings, Givaudan pretends that there is scientific uncertainty regarding whether diacetyl causes bronchiolitis obliterans. There is not. Neither the medical nor scientific community disagrees with NIOSH's conclusion that diacetyl causes bronchiolitis obliterans. This general acceptance alone carries substantial weight in favor of admitting Dr. Harrison's opinions. *Daubert v. Merrell Dow Pharm., Inc.*, 509 U.S. 579, 594, 113 S. Ct. 2786, 2797, 125 L. Ed. 2d 469 (1993) ("Widespread acceptance can be an important factor in ruling particular evidence admissible...").

**b) NIOSH has conducted numerous health hazard evaluations at microwave popcorn, flavoring, manufacturing, and other plants.**

NIOSH's doctors and scientists have repeatedly investigated, studied and published, detailed findings demonstrating the severe health risk to workers from exposure to diacetyl vapors in butter flavoring. As discussed above, in 2000, NIOSH reviewed medical records of

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<sup>5</sup> Comments to citizens and the NIOSH response are attached as Exh. 12 and available for review at <https://www.cdc.gov/niosh/docket/archive/pdfs/niosh-245/245-245-publicstakeholdercomments-10-31-16.pdf>

<sup>6</sup> Peer review comments with the NIOSH response are attached as Exh. 13 and available at <https://www.cdc.gov/niosh/docket/archive/pdfs/niosh-245/245-245-a-peerreviewcommentsdiacetyl2-3-pentanedione-10-31-16.pdf>

several Japer Popcorn Plant workers and determined that it should conduct a Health Hazard Evaluation of the plant. That Health Hazard Evaluation included spirometry tests, medical screening of workers, plant inspections, industrial hygiene studies, and air sampling. The work resulted in a peer-reviewed paper in August 2002 in the New England Journal of Medicine. Authors Kathleen Kreiss, M.D. of NIOSH's Division of Respiratory Disease Studies and her colleagues described their study at the Jasper Popcorn plant and concluded: "The excess rates of lung disease and lung-function abnormalities and the relation between exposure and outcomes in this working population indicate that they probably had occupational bronchiolitis obliterans **caused by the inhalation of volatile butter-flavoring ingredients**". (Exh. 14, *Clinical Bronchiolitis Obliterans in Workers at a Microwave Popcorn Plant*, New England Journal of Medicine at p. 330, Kreiss, et al., August 1, 2002)(emphasis added).

NIOSH followed that initial investigation at the Gilster Mary Lee popcorn plant with Health Hazard Evaluations at several other plants: Agrilink Foods Popcorn Plant, Ridgway, Illinois; ConAgra microwave popcorn plant, Marion, Ohio; Nebraska Popcorn, Clearwater, NE; and at American Pop Corn, Sioux City, Iowa.<sup>7</sup> (Exh. 11, at Chapter 2.5. Industrial Hygiene

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<sup>7</sup> Exh. 15, NIOSH [2003a]. Hazard evaluation and technical assistance report: Agrilink Foods Popcorn Plant, Ridgway, IL. By Sahakian N, Choe K, Boylstein R, Schleiff P. Cincinnati, OH: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, NIOSH HETA Report No. 2002-0408-2915.

Exh. 16, NIOSH [2003b]. Hazard evaluation and technical assistance report: Nebraska Popcorn, Clearwater, NE. By Kanwal R. Cincinnati, OH: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, NIOSH HETA Report No. 2002-0089.

Exh. 17, NIOSH [2004a]. Hazard evaluation and technical assistance report: American Pop Corn Company, Sioux City, IA. By Kanwal R, Boylstein R, Piacitelli C. Cincinnati, OH: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, NIOSH HETA Report No. 2001-0474-2943.

Exh. 18, NIOSH [2004b]. Hazard evaluation and technical assistance report: ConAgra Snack Foods, Marion, OH. By Kanwal R, Kullman G. Cincinnati, OH: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, NIOSH HETA Report No. 2003-0112-2949.

Exh. 19, NIOSH [2006]. Hazard evaluation and technical assistance report: Gilster-Mary Lee Corporation, Jasper, MO. By Kanwal R, Kullman G, Fedan K, Kreiss K. Cincinnati, OH: U.S. Department of Health and

Surveys and Exposure Assessments, pp. 22-32). NIOSH also conducted Health Hazard Evaluations at flavor manufacturing plants including: Carmi Flavor and Fragrance Company, Inc., Commerce, CA.; Gold Coast Ingredients, Inc., Commerce, CA; Agilex Flavors, Inc. formerly Key Essentials, Inc., Rancho Santa Margarita, CA; Chr. Hansen, Inc., New Berlin, WI; a flavor manufacturing plant in Indiana; and others.<sup>8</sup> *Id.* Each Health Hazard Evaluation is on the NIOSH website, included in the NIOSH Criteria Report, and is part of the basis for Dr. Harrison's opinions.

NIOSH collected the data and studied each plant individually and collectively which resulted in numerous published papers:

- Pendergrass SM. (2004). *Method development for the determination of diacetyl and acetoin at a microwave popcorn plant.* Environ Sci Technol 38(3): 858-61. [Exh. 25]
- Akpinar-Elci M, et al. (2004) *Bronchiolitis obliterans syndrome in*

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Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, NIOSH HETA Report No. 2000-0401-2991.

<sup>8</sup> Exh. 20, NIOSH [2007]. Hazard evaluation and technical assistance report: Carmi Flavor and Fragrance Company, Inc., Commerce, CA. By Kanwal R, Kullman G. Cincinnati, OH: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, NIOSH HETA Report No. 2006-0303-3043.

Exh. 21, NIOSH [2008a]. Evaluating occupational exposures and work practices at Agilex Flavors, Inc. formerly Key Essentials, Inc., Rancho Santa Margarita, CA. A technical assistance report to the California/Occupational Safety and Health Administration. By McKernan L, Dunn K. Cincinnati, OH: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, NIOSH HETA Report No. 2006-0361-2.

Exh. 22, NIOSH [2008b]. Hazard evaluation and technical assistance report: Gold Coast Ingredients, Inc., Commerce, CA. By Bailey R, McKernan L, Dunn K, Sahakian N, Kreiss K. Cincinnati, OH: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, NIOSH HETA Report No. 2007-0033-3074.

Exh. 23, NIOSH [2009]. Hazard evaluation and technical assistance report: Chr. Hansen, Inc., New Berlin, WI. By Sahakian N, Kullman G, Dunn K, Kanwal R. Cincinnati, OH: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, NIOSH HETA Report No. 2007-0327-3083.

Exh. 24, NIOSH [2011]. Hazard evaluation and technical assistance report: Lung function (spirometry) testing in employees at a flavorings manufacturing plant--Indiana. By Kreiss K, Piacitelli C, Cox-Ganser J. Morgantown, WV: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, NIOSH HETA Report No. 2008-0155-3131.



*popcorn production plant workers*, Eur Respir J 24: 298-302. [Exh. 26]

- Kullman G et al. (2005). *Characterization of respiratory exposures at a microwave popcorn plant with cases of bronchiolitis obliterans*. J Occup Environ Hyg 2: 169-78. [Exh. 27]
- Akpınar-Elci, et al., *Induced Sputum Evaluation in Microwave Popcorn Production Workers*, Chest 128: 991-997, at p. 991, August, 2005. [Exh.28]
- Kanwal, R et al. (2006). *Evaluation of flavorings-related lung disease risk at six microwave popcorn plants*. J Occup Environ Med 48(2): 149-57. [Exh. 29]
- Kreiss, K. (2007). *Occupational Bronchiolitis Obliterans Masquerading as COPD*. Am J Resp Crit Care Med 176: 427-429. [Exh. 30]
- Sahakian and Kreiss, *Lung Disease in Flavoring and Food Production: Learning from Butter Flavoring*, chapter in *Advances in Food and Nutrition Research*, Vol. 55, 2009. [Exh. 31]

NIOSH scientists are not the only scientists to have studied diacetyl. Scientists outside of NIOSH have also studied and written in the peer-reviewed literature on this subject. Dr. Parmet published his initial report in 2002. (Exh. 32, Parmet, AJ, Von Essen, S. (2002) *Rapidly progressive, fixed airway obstructive disease in popcorn workers: a new occupational pulmonary illness?* J Occup Environ Med 44: 216-218) Similarly, Dr. Harrison and the California Department of Health conducted an extensive study of flavor manufacturing plants in California leading to published articles and a state regulation:

- Harrison, R: et al. (2006). *Food flavoring workers with bronchiolitis obliterans following exposure to diacetyl, California*, May 15, 2006. (Exh. 7)
- Materna, B. (2007). *Summary of eight known cases of confirmed or obstructive lung disease in California food flavoring manufacturing workers*. (Exh. 33)
- Kim, T; Materna, B; Prudhomme, J; Fedan, K; Enright, PL; Sahakian, N; Windham, G; Kreiss, K; [2010]. *Industry-wide medical surveillance of California flavoring manufacturing workers: cross-sectional results*. Am J Ind Med 53(9):857–865. (Exh. 34).



In Holland, a flavor plant was studied and the findings reported: Van Rooy, F et al. (2007) *Bronchiolitis Obliterans Syndrome in Chemical Workers Producing Diacetyl for food flavorings*. Am J Rep Crit Care Med 176: 498-504. (Exh. 35) In addition, several flavor manufacturers (not including Givaudan, of course) retained National Jewish Medical Center for advice and certain testing relating to this issue. The inspections resulted in the published paper Martyny, JW; Van Dyke, MV; Arbuckle, S; Towle, M; Rose, CS [2008] *Diacetyl exposures in the flavor manufacturing industry*. J Occup Environ Hyg 5(11):679–688). (Exh. 36)

The NIOSH Criteria Report includes and endorses many of these peer-reviewed studies. These lengthy and exhaustive studies confirm that diacetyl causes lung disease. Dr. Harrison's reliance upon these studies provides further evidence that he has a sufficient basis to render general causation options.

**c) NIOSH's conclusions have been repeatedly confirmed through reliable, repeatable animal studies**

Animal studies are the bedrock of epidemiological evidence. Because ethics understandably prohibit intentionally exposing humans to potential toxic substances, animals are often used for investigative purposes. Scientists familiar with the biology of animals and their comparison with human biology conduct these studies. NIOSH conducted studies exposing animals to diacetyl and butter flavors. These studies provide further evidence that exposure to diacetyl vapors causes lung disease. "Concentrations of **butter flavoring vapors** that can occur during the manufacture of foods are associated with epithelial injury in the nasal passages and pulmonary airways of rats". (Exh. 37, *Necrosis of Nasal and Airway Epithelium in Rats Inhaling Vapors of Artificial Butter Flavoring*, Toxicology & Applied Pharmacology at p. 133, Hubbs, et

al., September 11, 2002)(emphasis added).

A 2004 study reported: "These findings suggest that acute exposure in diacetyl alone is sufficient in causes upper respiratory tract epithelial necrosis in rats at concentrations of 198.4 ppm or higher. (Exh. 38, Hubbs A, et al. *Inhalation toxicity of the flavoring agent diacetyl (2,3-butanedione) in the upper respiratory tract of rats*. Toxicol Sci. 2004; 78S1:438-439).

In 2008, the same authors published once more, again concluding that diacetyl causes lung disease:

Inhalation of butter flavoring vapors by food manufacturing workers causes an emerging lung disease clinically resembling bronchiolitis obliterans. Diacetyl . . . is a major component of these vapors. In rats, we investigated the toxicity of inhaled diacetyl . . . Diacetyl inhalation caused epithelial necrosis and suppurative inflammation in the nose, larynx, trachea, and bronchi . . . Both pulsed and continuous concentrations caused epithelial injury. . . These findings are consistent with the conclusion that inhaled diacetyl is a respiratory hazard.

(Exh. 39, Hubbs A, et al. *Respiratory Toxicologic Pathology of Inhaled Diacetyl (2,3-butanedione) in Sprague-Dawley rats*. Toxicol Sci. 2008; 1533-1601).

In 2010, NIOSH conducted a rat study that determined: "Human disease correlates with exposure to diacetyl . . . a component of butter itself and many butter flavorings." In that study, Hubbs looked at the impact on rats of 2,3-pentanedione, because of "the structural similarities to diacetyl." The report stated: "These findings indicate that inhaled 2,3-pentanedione, similar to diacetyl, injures airway epithelium of rats, predominantly in the nose, but also affects deeper airways." (See Exh. 40, Aff. of Allen Parmet; see also Exh. 41, Hubbs A, et al. *Airway epithelial toxicity of inhaled agent 2,3-pentanedione*. The Toxicologist (NIOSH), 114, S-1, pg 319, March 2010). Nor is Dr. Hubbs alone in her work with diacetyl and butter flavoring animal studies. In fact, as far back as 1993 another flavor company, BASF, conducted its own rat study. (Exh. 42, BASF (1993) *Study on inhalation toxicity of diacetyl FCC as a vapor in rats: 4 hour exposure*

(unpublished)).

The National Toxicology Program/National Institute of Environmental Health Sciences also conducted an animal study and concluded: “Finally, we would again emphasize that our results using exposures relevant to human workplace conditions demonstrate that diacetyl exposure in rodents lead to significant epithelial injury and lymphocytic airway inflammation which are known to precede the development of OB [obliterative bronchiolitis] in humans.” (Exh. 43, Morgan, et al. (2008) *Respiratory Toxicity of Diacetyl in C57B1/6 Mice*, Toxicological Sciences, Vol. 103, Issue 1pp. 169-180; *see also*, Exh. 44, Kelly, et al., *A Rodent Model of Toxin Induced Bronchiolitis Obliterans*, Am Journal Respiratory and Critical Care Medicine; 181; 2010; A1750).

The distinction Givaudan creates in its legal arguments to this Court simply does not exist in the scientific context.

**2. Dr. Harrison, like NIOSH, also utilized the Bradford-Hill criteria in confirming that diacetyl causes lung disease, giving yet another valid scientific basis for his general causation opinion.**

The leading test to assess causation is the Bradford Hill criteria. *See*, Hill AB [1965]. The environment and disease: association or causation? Proc R Soc Med 58:295–300. This criteria employs eight tests to assess causation:

- Temporality – the exposure precedes disease development;
- Strength of association – the magnitude of the apparent health risk due to exposure
- Replication of findings
- Consistency
- Biologic plausibility
- Dose-response relationship
- Consideration of alternate explanations

The methods of Sir Bradford Hill have been adopted and recognized as reliable for years in both scientific and medical endeavors. Courts around the United States, including those within the Eighth Circuit, have also held them to be scientifically valid. Just this year, the Eighth Circuit upheld a jury verdict in plaintiff's favor on the grounds that the defendant's TCE caused her autoimmune hepatitis. *Kirk v. Schaeffler Group USA, Inc.*, 887 F.3d 376, (8th Cir. 2018). The district court endorsed the Bradford Hill criteria as a reliable method to base general causation on: "Dr. Guzelian is well-qualified, and his report applies nine well-established guidelines, commonly known as the Bradford Hill criteria, to analyze whether TCE has been shown to cause AIH in humans." *Kirk v. Schaeffler Grp. USA, Inc.*, No. 3:13-CV-5032-DGK, 2015 WL 12426834, at \*2 (W.D. Mo. Sept. 29, 2015) (citing *In re Neurontin Mktg., Sales Practices, & Prods. Liab. Litig.*, 612 F. Supp. 2d 116, 132-33 (D. Mass. 2009) (observing courts have generally accepted the Bradford Hill criteria)).

Federal circuit courts agree that the Bradford Hill criteria are scientifically reliable. The Third Circuit holds: "The Bradford Hill criteria are broadly accepted criteria for evaluating causation that have been developed by scientists such as Sir Bradford Hill." *Gannon v. United States*, 292 F. App'x 170, 173 n.1 (3rd Cir. 2008). The Ninth Circuit echoes: "The Bradford Hill methodology refers to a set of criteria that are well accepted in the medical field for making causal judgments." *Wendell v. GlaxoSmithKline LLC*, 858 F.3d 1227, 1235 (9th Cir. 2017). And in 2011, the First Circuit reversed the district court's exclusion of plaintiff's causation expert, holding that his testimony was sufficiently reliable because "the sum of his testimony was that a weighing of the Hill factors, including biological plausibility, supported the inference that the association between benzene exposure and APL is genuine and causal." *Milward v. Acuity Specialty Prod. Grp., Inc.*, 639 F.3d 11, 26 (1st Cir. 2011).

In contrast, Givaudan cannot find a single case that questions the reliability of Bradford Hill. Givaudan ignores these criteria and hopes the Court will too. But the Court cannot ignore these criteria because NIOSH is clear that it uses them as a basis to establish causation:

Investigations of severe lung disease consistent with obliterative bronchiolitis among diacetyl-exposed employees have provided substantial evidence of a causal relationship between diacetyl exposure and development of this disease. Exposure preceded disease development, and lung disease risk decreased with control of exposures. Analyses of data from workplace medical and environmental surveys revealed a strong, consistent association of the disease with diacetyl manufacture, use of diacetyl in flavoring production, and use of diacetyl-containing butter flavorings in microwave popcorn production. The investigations have also shown evidence of a dose-response effect, and animal and other laboratory studies have provided evidence of biologic plausibility. Medical evaluations of affected employees did not identify alternative explanations for their illness besides their workplace exposure to diacetyl and other flavoring compounds. **Accordingly, the criteria for interpreting epidemiologic associations as causal have all been met by the body of investigation presented in this criteria document for a recommended standard.**

Exh. 11, at p. 74.

The fact that NIOSH utilized the Hill Criteria in its determination of causation ensures that the methodology underlying the NIOSH Criteria Report is reliable and satisfies *Daubert*. Further, as discussed above, Dr. Harrison independently applied and analyzed the Hill criteria to diacetyl. (Exh. 8). His opinions are based on accepted scientific methodology and cannot be excluded.

**D. Givaudan's critiques of Dr. Harrison's opinions do not render them inadmissible.**

The science is unequivocal: Exposure to butter flavoring with diacetyl causes lung disease including bronchiolitis obliterans. Nonetheless, Givaudan attempts to create uncertainty where none exists by raising three arguments as to why this Court should disregard the sound science supporting Dr. Harrison's general causation opinions. First, Givaudan cites to differences

in terminology and symptoms. But the literature Dr. Harrison relies on acknowledges the many different names bronchiolitis obliterans has gone by, as well as its various symptoms. Dr. Harrison has not made up a new, undocumented disease. Next, Givaudan attempts to sow confusion by arguing semantics surrounding exposure levels. The Eighth Circuit does not require Dr. Harrison to identify the precise level of exposure that will trigger disease. Nonetheless, he testified that anything above 5 parts per billion – a level far below what Mr. Herbst was exposed to – is an unsafe level. Finally, Givaudan selectively cites two studies, each from over a decade ago, to argue that the science is not settled. The language Givaudan focuses on does not contradict the conclusion that diacetyl causes bronchiolitis obliterans. Even if it did, though, it is still reversible error to exclude Dr. Harrison's opinions – the presence of competing scientific evidence raises a question of fact for the jury. Givaudan's criticism of Dr. Harrison's opinions, to the extent they have any merit, are fodder for cross examination. They cannot be the basis for exclusion.

**1. The name for the life-threatening disease caused by diacetyl has gone by different functional names but they are all the same disease.**

Givaudan knows that unless it convinces this Court to ignore the vast body of literature and studies set out above (and upon which Dr. Harrison relies), it cannot hope to exclude him. Therefore, it attempts a sleight of hand by arguing that Flavoring Induced Bronchiolitis Obliterans (FIBOS) and Flavoring Related Bronchiolitis Obliterans (FRBOS) are entirely different diseases from bronchiolitis obliterans. The truth is FIBOS, FRBOS, and bronchiolitis obliterans are the same disease. These names have developed to help treating doctors who encounter this rare disease to better recognize it. Indicating the actual cause, "flavoring," in the name itself is more likely to alert a physician performing a literature search.

Givaudan knows this is true and is very careful in its wordsmithing. It does not disclose to the Court that the scientific community has used different names for the disease throughout the discovery and investigation of this disease. NIOSH summarized that history in its NIOSH Criteria Report:

**Scientific publications** that have reported on the occurrence and natural history of the illness **have used different diagnostic terms including fixed obstructive lung disease** [CDC 2002], **popcorn worker's lung** [Schachter 2002], **flavorings-related lung disease** [Kanwal et al. 2006; NIOSH 2009a], **clinical bronchiolitis obliterans** [Kreiss et al. 2002], **bronchiolitis obliterans syndrome** [Akpinar-Elci et al. 2004], **and flavoring-related bronchiolitis obliterans** [Kreiss 2007]. Of the few surgical lung biopsies that have been performed in affected employees, some have been interpreted as showing evidence of “constrictive bronchiolitis” or “obliterative bronchiolitis” [Akpinar-Elci et al. 2004; Kanwal 2008]. The term *fixed obstructive lung disease* is the least specific of the terms. The term *popcorn worker's lung* refers to the population of employees in which the disease was first identified. The term *flavorings-related lung disease* refers to the full spectrum of lung diseases that may be related to flavorings exposure and is not necessarily limited to obstructive conditions. The terms *flavoring-related bronchiolitis obliterans*, *constrictive bronchiolitis*, and *obliterative bronchiolitis* refer to pathologic findings of inflammation and fibrosis primarily involving the bronchioles, leading to irreversible airflow limitation. Terminology is complicated by the fact that, historically, researchers have applied the term “bronchiolitis obliterans” to different distinct disorders that involve the bronchioles [King 2003; King and Kinder 2008]. The terms clinical bronchiolitis obliterans and bronchiolitis obliterans syndrome refer to those who are thought to suffer from this pathologic condition based on clinical findings, but have not undergone lung biopsy for pathological confirmation. Additional discussion regarding diagnostic terminology in relation to the different recognized forms of bronchiolitis is included in section 3.1.1.

(Exh. 11, pp. 43-45).

NIOSH concludes that discussion by saying:

Because the terminology used in the peer-reviewed literature of flavorings-exposed employees has included several different accepted and frequently interchanged diagnostic terms, and indeed may have been influenced by the peer-review process itself, this criteria document sometimes provides the terms used in the cited papers and includes the criteria used in the patient evaluations.

*Id.* at 45.

Even the award that Dr. Parmet, one of the doctors whose work Givaudan asks this Court to discredit, received in 2009 for discovering the link between bronchiolitis obliterans and diacetyl acknowledges the different names for the same disease. In its recognition of Dr. Parmet, the ACOEM stated:

- ***Allen J. Parmet, MD.*** This award is presented to recognize an ACOEM member for a specific or unique achievement in OEM. Dr. Parmet, in private practice in occupational medicine in Kansas City, Mo., was bestowed this award for identifying a new serious occupational disease - **variously termed popcorn packers lung, bronchiolitis obliterans syndrome, diacetyl-induced bronchiolitis obliterans, or flavoring-induced bronchiolitis obliterans.**

(Exh. 45)(emphasis added).

Additionally, Dr. Kathleen Kreiss, the lead investigator into this disease, described the biased attempts to challenge the term BOS as "largely semantic" and concluded that these attempts do not "affect the science of recent research on workers." (Exh. 46, Kreiss, K, et al., Re: Galbraith D and Weill D (2009), Popcorn lung and bronchiolitis obliterans: a critical appraisal, 83 Int. Arch. Occup. Environ. Health 467-469 (2010)).

Over the years, there have been different diagnostic terms utilized in the discussion of the same occupational disease at issue in this case. The differences are merely semantic and have no impact on the applicability of the scientific findings upon which Plaintiffs' experts rely. Thus, Givaudan's argument regarding the name of the disease is without merit.

## **2. Diacetyl exposure can create a spectrum of lung injury symptoms.**

The published literature does not agree with Givaudan's argument that because there is not uniform consistency in the symptoms of workers who have been exposed to diacetyl, there is no scientific basis to conclude that they share the same lung disease. Instead, the literature



documents the various symptoms, attributing them all to diacetyl:

“The spectrum of health effects related to flavorings may be broader than fixed obstruction. Asthma, bronchiolitis obliterans with organizing pneumonia, granulomatous pneumonitis, tracheo- and bronchiomalacia, fibrosis and systemic symptoms without obstruction have all been reported in flavoring-exposed workers.”

(Exh. 30, Kreiss, Occupational Bronchiolitis Obliterans Masquerading as COPD, American Journal of Respiratory and Critical Care Medicine, Vol. 176 at p. 428, 2007.).

In the NIOSH Criteria Report, NIOSH states:

“Although diacetyl causes obliterative bronchiolitis, a debilitating and potentially fatal condition, it may be associated with a spectrum of disorders. Clinical observations present a picture of largely obstructive disease with a combination of reduced FEV<sub>1</sub> and FEV<sub>1</sub>/FVC ratio. However, it may also cause restrictive ventilatory impairment, characterized by reduced FEV<sub>1</sub> and normal FEV<sub>1</sub>/FVC ratio [Akpinar-Elci et al. 2004; Kreiss 2007; Lockey et al. 2009].

(Exh. 11, at p. 104).

The NIOSH Criteria Report includes Chapter 3.1 entitled Obstructive Lung Disease Consistent with Obliterative Bronchiolitis which explains the most significant health findings involving diacetyl. *Id.* at p. 37. NIOSH states:

The most significant health consideration for flavoring-exposed employees is the development of exertional dyspnea or findings consistent with obliterative bronchiolitis (also often called constrictive bronchiolitis, see discussion of terminology). Most textbooks characterize obliterative bronchiolitis as a rare disease with airways obstruction, defined by a decreased FEV<sub>1</sub> and a decreased FEV<sub>1</sub> to FVC ratio on spirometry testing. The magnitude of decline in FEV<sub>1</sub> determines the severity of the disorder. However, three recent case series of biopsy-confirmed obliterative bronchiolitis document that many cases have normal spirometry and, when abnormal, the spirometric pattern can be restrictive, obstructive, or mixed restrictive and obstructive in nature [Ghanei et al. 2008; King et al. 2011; Markopoulou et al. 2002]. Because of the historical assumption that obliterative bronchiolitis is an obstructive disease, the early NIOSH investigations focused on obstructive abnormalities.

Airways obstruction can occur in diseases such as smoking-related COPD (including emphysema and chronic bronchitis) and in asthma. In emphysema, the

fixed (i.e., does not respond to bronchodilator medications), whereas in asthma, the airways obstruction is at least partially responsive to bronchodilators (reversible airways obstruction). Most employees who have developed obstructive lung disease while exposed to diacetyl and other flavoring compounds have had fixed airways obstruction. Additional medical tests in severely affected employees have generally revealed findings consistent with the irreversible obstructive lung disease obliterative bronchiolitis (discussed in detail in section 3.1.2). Serial lung function testing with spirometry indicates that affected employees can experience very rapid lung function declines.

*Id.* at pp. 37-43. NIOSH further offers a Table 3-12 which describes the flavoring health effects described in the scientific literature. *Id.* Elsewhere in the NIOSH Criteria Report NIOSH writes:

NIOSH now has evidence from several investigators outside of the flavoring lung disease field that the clinical spectrum of biopsy-confirmed obliterative bronchiolitis includes both restrictive spirometry and normal spirometry, as well as those with fixed obstructive spirometry.

*Id.* at p. 59.

In a recent deposition in another case against Givaudan involving workers at an Ohio ConAgra microwave popcorn plant, Dr. Pue explained that the term “FIBOS” does not indicate a break with the research, science, or methodology related to diacetyl and bronchiolitis obliterans:

Q. Flavoring-related bronchiolitis obliterans, as a term, is meant to be more specific and descriptive in part to help clinicians as they review a subset of folks that have BO; is that correct?

A. Yes. The -- let me just explain it this way, is the original descriptions of bronchiolitis obliterans and what I was aware of when I was in my training were the high-level, high-dose exposure acutely, that result in acute lung injury and subsequent scar tissue, and the transplant patients, both bone marrow transplant patients and in lung transplant patients, which I did both of those when I was in my training.

Over time, like with any disease process, you find little side parts of the disease that are a little bit different than the primary initial description, but it's still the same disease. It's still bronchiolitis obliterans. It just has little twists and turns.

And when you look at this particular subset of bronchiolitis obliterans, this is the group that have low-level, long-term exposure causing lung injury, which results in inflammation, some bronchoreactivity, some obstruction, and some restriction.

So these changes are just a little bit different than what was the classical description of bronchiolitis obliterans, but it's a subset of the original diagnosis. And that's why if you look at the literature and you look at Dr. King's paper, and you look at Dr. Kreiss' work, they're not saying this is a new disease process. They're just saying within this subgroup of bronchiolitis obliterans, this looks a bit different.

Q. And that's not only -- and that's consistent with what you've seen in your own clinician work, as well as as a expert in the last few years, correct?

A. Yes, because when I first started seeing these patients back in the mid to late 2000s, before 2011, 2012, when I really wasn't seeing too many more clinically at that point, they just looked a little bit different than the classic description of bronchiolitis obliterans that I was familiar with, and I was having trouble kind of pulling that all together.

And as time went by, it crystallized for me. And then other people started writing about the same thing at the -- after that, saying, look, there is some reversibility of airflow; there -- you know, if you take them out of exposure, they can have some improvement; you can have some inflammatory component that can respond to anti-inflammatory therapy, which is different -- it's a different subset than the original description of bronchiolitis obliterans but it's still the same disease process.

It's just an evolving disease process, rather than the final end point of bronchiolitis obliterans.

(Exh. 47, Deposition of Dr. Pue, 332:1-335:9).

Likewise, Dr. Parmet offered the analogy of the difference between a first-degree and third-degree burn to explain why a spectrum of lung disease is observed in workers exposed to diacetyl:

Q. So earlier today I thought you said FIBO was in your opinion a separate disease process than BO.

A. I don't think it's separate. What I think it is, it's a continuum that's caused by cell death and inflammation that will lead to fibrosis and an irreversible state that's called bronchiolitis obliterans.

Q. How is that different than classic BO?

A. That's what that is. Whereas, if you just have some inflammation, that's reversible. **If I can use the analogy, if you get a burn and it's a first**

**degree burn, that's reversible. That will not leave a scar. But if you get a third degree burn and you kill cells, you will have a scar. That's now irreversible. Those are spectrum of the same condition.**

Q. Well, classic BO, if you set aside flavoring-induced BO, classic BO, does it not start out the same way?

A. It does but it's typically a single exposure that produces the result with a massive cell death. This is not a single exposure. This is a continual low level exposure with continuing irritation and death on a chronic basis. And because of the chronicity of this, I think we see cell repair, regeneration and a spectrum of the disease that you don't see with a sudden exposure in something like nitrogen tetroxide or mustard gas.

(Exh. 48, Parmet Dep., *Aregood*, 169:2-170:6)(emphasis added).

Hence, the fact that individuals experience a spectrum of symptoms is not unusual and does not nullify the science establishing that diacetyl causes lung disease.

Givaudan also argues that because the original cases seen by Dr. Parmet and NIOSH have not received lung transplants this somehow proves that the diagnoses wrong. NIOSH has described lung transplants among flavor exposed workers. Describing the initial Jasper workers, NIOSH states:

All nine employees had been prescribed oral corticosteroids, but none had improvement in lung function. Five of the employees had been placed on lung transplant waiting lists by their personal physicians [Akpinar-Elci et al. 2004].

(Exh. 11, at p. 46). Elsewhere, NIOSH stated:

Some affected employees have been placed on lung transplant waiting lists by their physicians because of the severity of their disease [Akpinar-Elci et al. 2004], and some flavoring-exposed employees have received lung transplants. p. 71.

*Id.* at p. 71.

Lung transplants create their own dilemma – the body does not readily accept the new lung requiring lifetime anti-rejection medicines and, more important, lung transplant recipients have a very short life expectancy. Most do not survive five years. As such, it is best to delay a

transplant if it can be done, no matter the diagnosis.

**3. Dr. Harrison properly accounts for the unsafe level of exposure.**

Givaudan also attacks Dr. Harrison's general causation opinion by claiming that he cannot identify the precise level of exposure that will cause lung disease. But the Eighth Circuit has never required that an expert give such precise exposure levels before he can offer his opinions to the jury. In *Bonner*, the court held that a plaintiff does "not need to produce a mathematically precise table equating levels of exposure with levels of harm in order to show that she was exposed to a toxic level of [defendant's product]." *Bonner v. ISP Technologies, Inc.*, 259 F.3d 924, 928 (8th Cir. 2001). Bonner's expert "was unable to offer a threshold exposure amount for injury to occur [and] failed to determine how much FoamFlush Bonner was exposed to." *Bonner*, 259 F.3d at 932. The Eighth Circuit rejected the argument that an expert cannot testify unless he can identify the threshold unsafe level of exposure. It affirmed that the expert's opinion satisfied the *Daubert* standard, noting that the expert explained that "as small as a quarter of a teaspoon can have toxic effects, and that inhalation is a more potent exposure mechanism than is ingestion." *Id.* This testimony sufficiently constituted "evidence from which a reasonable person could conclude that the exposure probably caused her injuries." *Id.*

Dr. Harrison testified based on the scientific literature that exposure to levels above 5 parts per billion ("ppb") would likely cause bronchiolitis obliterans:

Q. You say in your report that these results show that more than a decade after the food flavoring industry should have been aware of the toxicity of diacetyl and other food flavorings, exposures to diacetyl were above the NIOSH recommended limit of 5 parts per billion. These levels of diacetyl in the workplace at the ConAgra plant, Rensselaer, posed a substantial risk of bronchiolitis obliterans and other lung disease. Is that the opinion that you intend to offer?

A. Yes.

Q. You are not saying that those levels were actually at a level -- those exposures were actually at a level that was likely to cause BO or other lung disease, just that they posed a substantial risk of BO or other lung disease; is that correct?

A. I don't understand the difference between likely and pose a substantial risk. To me they mean the same thing.

Q. Okay. Do you have an opinion of the level of exposure to diacetyl that is likely to cause disease -- lung disease in people?

A. Anything over five parts per billion poses a substantial risk.

Q. Okay.

A. And can cause lung disease. The word "likely," I -- I'm using in the same way that I would say poses a substantial risk.

Q. Okay.

A. It doesn't mean that it causes lung disease in everybody.

Q. And, for -- for your opinion that -- that exposures over five parts per billion is likely to cause lung disease, or can cause -- or poses a substantial risk of lung disease, you're relying on the NIOSH REL [Recommended Exposure Limit] of five parts per billion in 2016?

A. If you ask me about what level, yes, that's correct.

(Exh. 49, Deposition of Dr. Harrison, 125:6-126:18).

This testimony is consistent with the opinions he offered in his written report, where he discusses the studies of diacetyl levels in popcorn plants such as the one Mr. Herbst worked in:

Diacetyl levels ranged from the limit of detection (< 0.01 ppm) to as high as 60 ppm, with a mean of 1.80 ppm and a median of 0.10 ppm. These mean and median levels are substantially higher than the NIOSH Recommended Exposure Limit (REL) of 5 ppb and are similar to the diacetyl levels in those plants where cases of severe lung disease have occurred.

(Exh. 8, p. 29, citing Martyny, J. W., Van Dyke, M. V., Arbuckle, S., Towle, M., & Rose, C. S. (2008). *Diacetyl exposures in the flavor manufacturing industry*. Journal of Occupational and Environmental Hygiene, 5(11), 679-688.)

Givaudan nonetheless argues that because NIOSH set 5 ppb as the safe occupational exposure limit, Dr. Harrison cannot refer to it to support his causation opinions. Once again, Givaudan presents an argument that has been consistently rejected by the Eighth Circuit. In *Kirk*, the Eighth Circuit held that there is “little doubt” that regulatory standards are “probative evidence” of causation. *Kirk*, 887 F.3d, at 392, *see also Yates v. Ford Motor Co.*, No. 5:12-CV-752-FL, 2015 WL 2189774, at \*15 (E.D.N.C. May 11, 2015) (the EPA is assumed to be an objective government body . . . the fact that the EPA accepted the position that brake asbestos could cause lung disease makes it more likely that those studies supporting a link between brake asbestos and lung disease are valid.”). And because of the clear evidentiary value governmental standards have, they cannot be excluded. Instead, the Eighth Circuit holds that experts must be permitted to discuss these standards, and defendants can request a limiting instruction if they desire: “the district court properly instructed that ‘exceeding these numbers does not in and of itself establish causation.’ There was no abuse of the court's discretion in fashioning appropriate instructions.” *Kirk*, 887 F.3d, at 392.

This Court cannot exclude Dr. Harrison’s opinions based on the collateral issues of whether or not exposures above 5 ppb are “unsafe” or create a “likely” risk of lung disease as opposed to a “substantial” one. Both Dr. Harrison and Dr. Pue have reviewed the diacetyl measurements performed at the plant. Dr. Pue has even taken a history directly from Mr. Herbst concerning his diacetyl exposure. It is clear that he was exposed to diacetyl at a level significant enough to cause his disease and much higher than the threshold level Givaudan faults Dr. Harrison for failing to pinpoint. Givaudan presents no grounds to exclude Dr. Harrison’s causation opinions.

**4. NIOSH has created a peer-reviewed formula to accurately interpret results from studies utilizing Method 2557.**

Givaudan is wrong when it claims that any studies utilizing Method 2557 are unreliable and fatally flawed. NIOSH has developed a peer-reviewed formula for accurately converting Method 2557 measurements into reliable results. NIOSH originally used Method 2557 to analyze air samples beginning in 2000 at the Jasper, MO microwave popcorn plant. Over the next half decade, numerous Health Hazard Evaluations (“HHEs”) were performed at flavoring plants across the country using Method 2557. But in 2007, NIOSH determined that humidity could impact the sampling and result in an “underestimate of the true diacetyl concentrations.” Exh. 11, at 17. NIOSH responded by first developing a new method of conducting air samples and next engaging in rigorous research to determine if the measurements taken via Method 2557 could still be relied on. NIOSH concluded these measurements were still reliable: “NIOSH researchers worked extensively to understand this problem and derive an appropriate correction for estimating diacetyl levels [Cox-Ganser et al. 2011]. This correction, based on absolute humidity and time to extraction, was applied to the diacetyl exposure levels above the limit of detection (LOD) as measured in the selected HHEs.” Exh. 11, at p. 107.

By running experiments and conducting tests in a laboratory capable of permitting NIOSH’s team of scientists to adjust air temperature, relative humidity, and diacetyl concentration, NIOSH was able to develop a mathematical formula that could reliably convert Method 2557 results into accurate measurements. *Id.* This research and formula was peer-reviewed and published in *Correcting Diacetyl Concentrations from Air Samples Collected with NIOSH Method 2557*, Cox-Ganser, et al., J. of Occupational and Environmental Hygiene, 8:59-70 (2011) at p. 59. NIOSH now has a tested method to assess the risks of exposure to various levels of diacetyl, even when those levels had been measured using Method 2557:



We derived a mathematical correction procedure to more accurately estimate historical workplace diacetyl concentration based on laboratory-reported concentrations of diacetyl using Method 2557, and sample site temperature and relative humidity (to calculate absolute humidity), as well as days of sample storage prior to extraction in the laboratory. With this correction procedure, quantitative risk assessment for diacetyl can proceed using corrected exposure levels for air samples previously collected and analyzed using NIOSH Method 2557 for airborne diacetyl.

(Exh. 11, at Appendix F, *Correcting Diacetyl Concentrations from Air Samples Collected with NIOSH Method 2557*, Cox-Ganser, et al., J. of Occupational and Environmental Hygiene, 8:59-70 (2011) at p. 59)

The NIOSH Criteria Report also contains Table 2-1 entitled: “Multiple investigations of diacetyl in flavoring and food production industries.” This table includes the studies of diacetyl and lung disease conducted at flavoring plants across the country and confirms that those studies that employed Method 2557 have been corrected using the formula. *Id.* at p. 24.

Neither Mr. Herbst’s counsel nor his expert have ever questioned the accuracy of this formula. In the case mentioned by Givaudan, *Watson v. Dillon Companies, Inc., et al.*, while Plaintiff’s counsel did seek to exclude results collected via Method 2557 based on their unreliability, the thrust of their argument was that defendants’ experts had not applied the corrective formula that has been applied in this case: “Mr. Bacci ignored the peer-reviewed, generally-accepted calculation for correcting Dr. Martyny’s diacetyl measurements under Method 2557 to ensure they are accurate.” (Exh. 50, Plaintiff’s Objections to all Evidence of and References to NIOSH Method 2557, at 7) Givaudan, of course, ignores this part of Plaintiff’s counsel’s argument and emphasizes only that Plaintiff’s counsel called Method 2557 unreliable. But Givaudan’s insistent focus on the “unreliability” of Method 2557 to the exclusion of the known, peer-reviewed, and accepted formula to correct results obtained via Method 2557 cannot change the reality that because this formula exists, samples measured via Method 2557 are still

able to be relied on by the scientific community. Likewise, Dr. Harrison determined that NIOSH's results and 2016 Criteria Report are accurate. He testified that NIOSH's scientists "went through an incredible amount of scrutiny to get their papers published by the 'New England Journal' and other prestigious journals." Exh. 49, 52:5-23. He is "satisfied" that "they did it right" and "recognized the scientific challenges and corrected it." Exh. 49, 62:2-63:1. His reliance on studies that utilize Method 2557 cannot be excluded.

**5. None of the studies Dr. Harrison relies on concludes that diacetyl does not cause lung disease, but even if one did, only the jury can weigh the merits of competing scientific studies.**

Rather than acknowledging the overwhelming scientific literature behind Dr. Harrison's opinions, buttressed by the fact that both Dr. Harrison and NIOSH have applied the Bradford Hill criteria to conclude that diacetyl causes lung disease, Givaudan claims that no scientific literature supports his conclusion. To support this inaccurate claim, Givaudan cites only two articles, one published in 2002, and the other in 2006. Neither of these articles contradict the conclusion that diacetyl causes lung disease. The 2002 article states that "diacetyl may be a cause of lung disease" and the 2006 article concludes that more data is needed before establishing "workplace exposure standards or recommended exposure limits for butter flavorings." Like NIOSH, Dr. Harrison considered both of these articles in reaching his opinion that diacetyl causes lung disease. They are each one of many peer-reviewed articles on the subject within the scientific literature that when taken as a whole overwhelmingly establish causation. Givaudan's contention that these articles contradict the consensus within the scientific community that diacetyl causes lung disease is wrong.

Yet even if these articles conclude (and they do not) that diacetyl does not cause lung disease, they would still not render Dr. Harrison's opinion inadmissible. The Eighth Circuit holds

that only a jury can decide between competing views within the scientific community. As explained above, the Eighth Circuit “admonishes” district courts “not to weigh or assess the correctness of competing expert opinions.” *Johnson*, 754 F.3d at 562. Instead, even in the face of conflicting evidence, a district court cannot exclude an expert’s opinion unless “it is so fundamentally unsupported that it can offer no assistance to the jury.” *Wood v. Minn. Mining & Mfg. Co.*, 112 F.3d 306, 309 (8th Cir.1997).

Far from being fundamentally unsupported, Dr. Harrison’s opinion enjoys the support of over fifteen years of peer-reviewed scientific research including animal studies and studies performed at flavor plants like the one in this case. Two articles, each one over a decade old, that contain language that arguable can be interpreted to suggest that further study is needed cannot nullify the admissibility of Dr. Harrison’s opinion. At best the language Givaudan cites can be used on cross examination.

Givaudan cannot present a single study (peer-reviewed or otherwise) concluding that diacetyl does not cause bronchiolitis obliterans. Nor does it provide any articles concluding the unsafe threshold of exposure is much higher than what Plaintiff was exposed to. Yet Givaudan asks the Court to step into the jury’s shoes and weigh the merits of the competing scientific literature. But there is no debate in the scientific community and no “side” for the Court to choose, even if it was tempted to do so. Nonetheless, if Givaudan’s argument is to be believed and the literature, articles, and studies that unanimously conclude that diacetyl causes bronchiolitis obliterans, such a decision can only be reached by the trier of fact, not this Court. It would be reversible error to exclude the Dr. Harrison’s causation testimony and opinions.

#### **IV. CONCLUSION**

The inescapable conclusion that flows from reviewing the law and the science is that this Court cannot grant Givaudan’s motion. The Eighth Circuit holds that Dr. Harrison does not need

to cite published studies in support of his opinion. Yet Givaudan asks this Court to exclude his testimony even though he cites to numerous such studies. The Eighth Circuit holds that Dr. Harrison does not need to identify the specific level at which diacetyl causes harm. Yet Givaudan asks this Court to exclude his testimony even though he identifies any level above 5 parts per billion as creating a significant risk of lung disease. The Eighth Circuit holds that Dr. Harrison's opinion is admissible if it is based on methodology accepted by the scientific community. Yet Givaudan asks this Court to exclude Dr. Harrison's testimony even though he basis his opinion on his application of the Bradford Hill criteria, which is widely accepted by the scientific community. The Eighth Circuit admonishes district courts to liberally admit scientific testimony and allow the jury to decide between competing scientific viewpoints. Yet Givaudan asks this Court to exclude Dr. Harrison's opinions based on minor quarrels it has with a tiny fraction of the published studies.

Mr. Herbst has a lung disease because Givaudan sold a dangerous product. He has a right to present his evidence on causation to a jury. Givaudan's motion must be denied.

Respectfully submitted,

*s/ J'Nan C. Kimak*

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## **CERTIFICATE OF SERVICE**

I hereby certify that on this 5th day of October, 2018, I electronically filed the foregoing with the Court using the Court's CM/ECF system which sends notification of same to all counsel of record also listed below:

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